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CLINICAL RESEARCH

Symptom-to-needle times in ST-segment elevation myocardial infarction: Shortest route to a primary coronary intervention facility

Comparaison des délais de coronarographie selon la filière de prise en charge

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Summary

Background. — Primary percutaneous coronary intervention (PCI) is the preferred management for patients with acute ST-segment elevation myocardial infarction (STEMI) if performed in a timely manner by experienced providers. Patients can access a PCI facility by three routes: prehospital STEMI diagnosis by emergency medical services (EMS) and direct transport by EMS to a PCI facility (EMS-PCI); visit to a hospital emergency department (ED) followed by referral to an on-site PCI facility (ED-PCI); or transfer from the ED to a PCI facility in another hospital (ED-transfer-PCI).

Aims. — To assess the implementation rate in France of the guidelines recommending that STEMI patients be transported by EMS to a PCI facility and to compare the times between symptom onset and PCI for these three routes.

Methods. — We used the results of the pilot testing of a national quality indicator programme on STEMI in 64 hospitals, providing data on patient characteristics, referral route and symptom-onset-to-needle time. We compared delays for each route in a Cox proportional-hazard model.

Results. — In a population of 1217 patients, median symptom-onset-to-needle time was 186 minutes (Q1 133; Q3 292) for the EMS-PCI route, 237 minutes (Q1 165; Q3 368) for the ED-PCI route and 305 minutes (Q1 230; Q3 570) for the ED-transfer-PCI route. A total of 70.8% of

Abbreviations: AMI, acute myocardial infarction; ED, emergency department; EMS, emergency medical services; HR, hazard ratio; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

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patients were transported by EMS as recommended. After adjustment for age, symptom onset period (weekends/nights) and history of cardiovascular disease, the EMS-PCI route was associated with the shortest symptom-onset-to-needle times. The hazard ratio was 0.71 [0.59–0.86] for the ED-PCI route and 0.67 [0.52–0.86] for the ED-transfer-PCI route.

Conclusion. — STEMI patients receive prompter care after prehospital diagnosis and direct transport to a PCI facility by EMS than by visiting a hospital ED. Use of this referral route should be further encouraged in France as approximately one-third of STEMI patients are still presenting directly to the ED.

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Résumé

Contexte. — La prise en charge de l'infarctus du myocarde (IDM) sur la mise en œuvre d'une stratégie de reperfusion coronaire la plus précoce possible, en générale par angioplastie si elle peut être accomplie à temps par des opérateurs entraînés. En France, plusieurs filières de prise en charge ont été identifiées. La filière recommandée s'appuie sur l'appel au samu-centre 15, déclenchant l'envoi d'un effecteur qui effectue un diagnostic pré-hospitalier et amène le patient dans un établissement hospitalier avec une salle de coronarographie diagnostique et interventionnelle (SCDI). Cependant, d'autres filières existent. En effet, certains patients se présentent directement aux urgences des établissements hospitaliers et sont soit pris en charge dans l'établissement lorsque celui-ci dispose d'une SCDI, soit transféré dans un établissement en disposant.

Objectifs. — L'objectif de cette étude est de comparer les délais de prise en charge entre les symptômes et la ponction d'angioplastie selon la filière empruntée par le patient.

Méthodes. — Les données issues de l'évaluation de la qualité de la prise en charge de l'IDM dans 64 établissements hospitaliers ont été utilisées. Celles-ci comportaient les caractéristiques des patients prises en charge, les filières suivies, et les délais de prise en charge définis comme le délai entre les symptômes et la ponction d'angioplastie. Les filières ont été comparées à l'aide d'un modèle à risque proportionnel.

Résultats. — Parmi les 1217 patients inclus, le délai moyen de prise en charge était de 186 minutes (Q1 133 ; Q3 292) pour la filière recommandée comparée à 237 minutes (Q1 165 ; Q3 368) et 305 minutes (Q1 230 ; Q3 570) pour les patients se présentant directement aux urgences respectivement d'un établissement hospitalier avec et sans SCDI. Au total, 70,8 % des patients ont suivi la filière recommandée. Après avoir ajusté sur l'âge, la période de prise en charge (week-end et nuit) et les antécédents cardiovasculaires, la filière recommandée était associée au délai de prise en charge le plus court comparé aux filières passant par les urgences des établissements avec et sans SCDI (*Hazard ratio* de 0,71 [0,59–0,86] et 0,67 [0,52–0,86] respectivement).

Conclusion. — Les patients pris en charge dans la filière recommandée reçoivent des soins plus précoces comparés aux autres filières. Cependant, dans notre étude, un tiers des patients n'ont pas suivi la filière recommandée, ce qui suggère que davantage d'efforts d'éducation doivent être fait auprès de la population.

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Introduction

Primary percutaneous coronary intervention (PCI) is the preferred management strategy for patients with ST-segment elevation myocardial infarction (STEMI) if it can be performed in a timely manner by experienced providers; the shorter the delay to PCI, the higher the likelihood of survival [1–3]. It is therefore essential that patients with STEMI symptoms be diagnosed and referred to a PCI facility as quickly as possible. In international studies, prehospital STEMI diagnosis and direct access to a PCI facility reduced delays and improved clinical outcomes [4–6].

In France, patients with symptoms of STEMI can be referred to a PCI facility by calling an emergency phone number and, on instructions from the call-centre physician,

be transported directly to a PCI facility by the emergency medical services (EMS). A mobile intensive care unit manned by a nurse and emergency physician who can carry out the prehospital diagnosis of STEMI is dispatched on site. Alternatively, patients can arrive directly at the emergency department (ED) of a nearby hospital for a diagnosis of STEMI. From there, they can be referred to an on-site PCI facility, if available, or be transferred to a PCI facility in another hospital. Current guidelines recommend that patients call the emergency number in order to be transported by the mobile intensive care unit to the closest available PCI facility [7]. To our knowledge, however, no studies have compared times taken to access PCI by each of these routes in the French context.

The results of the pilot testing of the national quality indicator programme for STEMI care provide the opportunity to confirm that prehospital diagnosis leads to reduced delays in France. Furthermore, it provides an evaluation of the implementation rate in France of the guidelines [7] recommending that STEMI patients be transported by EMS to a PCI facility.

Methods

Context

The Haute Autorité de Santé is currently implementing a national indicator programme on quality of care for several pathologies, including STEMI. A pilot test of the STEMI quality indicators, developed by COMPAQHPST [8], the Haute Autorité de Santé and the French College of Cardiology, took place in 2010 in a sample of French hospitals. A total of 64 PCI-capable volunteer hospitals took part in the quality assessment (16 public teaching hospitals, 27 public general hospitals, 21 private hospitals). The hospitals were located throughout France.

Study population

Our study was based on data obtained during the assessment of the quality of care delivered to patients with acute myocardial infarction (AMI) in the hospital sample. Patients were included in our study if they were diagnosed with STEMI, if < 12 hours had elapsed from symptom onset to diagnosis and if they underwent primary PCI. Patients were excluded if the PCI referral route and data for calculating symptom-onset-to-needle time had not been recorded in their file. For eligibility, patients had to be hospitalized for > 24 hours in 2010 with a diagnosis of AMI (diagnosis codes I21 or I22 ICM-10). A random sample of 80 patient files was selected in each hospital or, if there were fewer than 80 files available in any hospital, all available files were selected. The sample size was chosen to limit the burden of data collection [9]. Anonymized data were collected retrospectively from the files by hospital staff. Informed consent was waived because the data were analysed anonymously.

Measures

The primary endpoint was time elapsed between STEMI symptom onset and PCI needle time ("symptom-onset-to-needle time") for: direct transportation to a PCI facility by EMS (EMS-PCI); referral by the ED to an on-site PCI facility (ED-PCI); and transfer from ED to PCI facility in another hospital (ED-transfer-PCI).

We defined needle time as the time of the arterial puncture for PCI. Symptom-onset-to-contact and contact-to-needle times were calculated for the EMS-PCI and ED-PCI routes, considering first medical contact time as EMS arrival time or patient arrival time at the hospital ED (data unavailable for ED-transfer-PCI route patients). Other recorded variables were patient age, period of onset (weekends [Saturday or Sunday] or nights [6.00 pm to 8.00 am on following day]) and history of cardiovascular disease as

given by any ongoing antiplatelet treatment (aspirin or clopidogrel).

Statistical analysis

Continuous variables are reported as means with standard deviations and categorical variables as numbers with percentages. Times are given as medians with first and last quartiles. Differences in patients' characteristics between included and excluded patients and between referral routes were tested by univariate analysis using Student's *t* test or Pearson's chi-square test, as appropriate.

We first analysed symptom-onset-to-needle time using the PCI referral route as covariate in a Cox proportional-hazard model after stratification on the hospital where PCI was performed. Analyses were adjusted for age, weekend or night onset and history of cardiovascular disease. No data were censored as all patients underwent PCI. We calculated a point estimate and two-sided 95% confidence interval for the hazard ratio (HR). We then added symptom-onset-to-contact time for the EMS-PCI and ED-PCI routes as a covariate to the model.

We also tested for potential differences in symptom-onset-to-needle time and symptom-onset-to-contact time between hospital status and activity level using Student's *t* test.

All *P* values are two-sided. A *P* value < 0.05 was considered significant. We used SAS software, version 9.2 (SAS Institute, Cary, NC, USA).

Results

Characteristics of patients and features of STEMI

A total of 4290 patients with a diagnosis of AMI were randomly selected for a quality of care assessment in the 64 participating hospitals. Of these 4290 patients, only 1754 met the inclusion criteria (diagnosis of STEMI, time of symptom onset or interval between onset and diagnosis < 12 hours, PCI as primary treatment). Of these patients, 537 were excluded because of missing data (unavailable symptom-onset-to-needle time or referral route). This left 1217 included patients (69% of eligible patients) for the analysis.

Compared with the 537 excluded patients, the 1217 included patients were younger (Table 1). There was no significant difference between included and excluded patients in terms of medical history of cardiovascular disease. The percentage of patients transported directly to a PCI facility by EMS was higher among included patients (70.8% vs 63.1%) and the percentage making their way to the ED was lower (Table 1). A higher percentage experienced symptom onset at weekends (30.2% vs 23.7%) and a lower percentage at nights (50.9% vs 70.6%).

Overall, fewer than half of the patients had a contact-to-needle time < 90 minutes, as recommended by the current guidelines (Table 2). Patients making their way to the ED and referred to an on-site PCI facility had a higher percentage of contact-to-needle time < 90 minutes (68.2%) than patients transported by EMS to a PCI facility (56.4%). However,

Table 1 Included and excluded patient characteristics.

	Included patients (n = 1217)	Excluded patients (n = 537)	P
Mean age (years)	63.1 ± 13.7	65.4 ± 14.9	0.001
PCI referral route			
EMS-PCI	862 (70.8)	316 (63.1)	0.005
ED-PCI	192 (15.8)	106 (21.2)	
ED-transfer-PCI	163 (13.4)	79 (15.8)	
Onset period			
Weekend	367 (30.2)	127 (23.7)	0.005
Night	620 (50.9)	379 (70.6)	< 0.001
History of cardiovascular disease			
Yes	221 (18.2)	116 (21.6)	0.09
No	996 (81.8)	421 (78.4)	

Data are mean ± standard deviation or number (%).

when considering a threshold of 120 minutes, no differences remained between the EMS-PCI and ED-PCI referral routes (76.5 vs 77.8; $P = 0.13$).

Delays according to referral route

Of the 1217 included patients, 862 were transported by EMS directly to a PCI facility, 192 were referred by the ED to an on-site PCI facility and 163 were transferred from the ED to another hospital. There were no differences in patient age, period of symptom onset (weekend or night), history of cardiovascular disease or referred hospital status between the three referral routes (Table 2). Symptom-onset-to-needle

time was lower for EMS transport than for on-site referral or between-hospital transfer (median time: 186, 237, and 305 minutes, respectively) (Table 3). Symptom-to-contact time did not differ between patients calling the EMS and those making their way to the hospital ED (patient subgroup referred to an on-site PCI facility) (90 vs 135 minutes) (Table 3).

Influence of referral route on symptom-onset-to-needle time

PCI referral route was an independent predictor of symptom-onset-to-needle time after adjusting for age, period of

Table 2 Patient characteristics according to referral route.

	EMS-PCI (n = 862)	ED-PCI (n = 192)	ED-transfer-PCI (n = 163)	P
Mean age (years)	62.6 ± 13.4	59.6 ± 13.9	60.9 ± 15.0	0.21
Onset period				
Weekend	262 (30.4)	56 (29.2)	49 (30.1)	0.94
Night	433 (50.2)	111 (57.8)	76 (46.6)	0.08
History of cardiovascular disease				
Yes	167 (24.0)	28 (17.1)	26 (19.0)	0.22
No	695 (80.6)	164 (85.4)	137 (84.0)	
Referred hospital status				
Teaching	261 (30.3)	57 (29.7)	58 (35.6)	0.08
Non-teaching public	324 (37.6)	86 (44.8)	50 (30.7)	
Private	277 (32.1)	49 (25.5)	55 (33.7)	
Contact-to-needle time ^a				
< 90 minutes	457 (56.4)	120 (68.2)	— ^b	< 0.001
< 120 minutes	620 (76.5)	137 (77.8)	— ^b	0.13

Data are mean ± standard deviation or number (%). ED: emergency department; EMS: emergency medical services; PCI: percutaneous coronary intervention.

^a Sum of column is different from number of included patients because of missing data for time of first medical contact.

^b Time of first medical contact not available for ED-transfer-PCI referral route.

Table 3 Symptom-onset-to-needle and symptom-to-contact times.

	Symptom-onset-to-needle time (minutes)	<i>P</i>	Symptom-onset-to-contact time (minutes)	<i>P</i>
Hospital status				
Teaching (<i>n</i> = 16)	271 (253–333)	0.31	149 (129–166)	0.70
Non-teaching public (<i>n</i> = 25)	250 (199–307)		151 (111–185)	
Private (<i>n</i> = 21)	291 (225–338)		155 (131–96)	
Activity level (cases per year)				
0–55	238 (195–335)	0.35	183 (116–251)	0.12
56–121	250 (219–287)		140 (128–170)	
122–184	301 (216–328)		153 (109–183)	
185–434	280 (258–370)		149 (135–165)	
Referral route				
EMS-PCI	186 (133–292)	0.002	90 (50–180)	0.15
ED-PCI	237 (165–368)		135 (63–228)	
ED-transfer-PCI	305 (230–570)		Data NA	

Data are median (Q1–Q3). ED: emergency department; EMS: emergency medical services; NA: not available; PCI: percutaneous coronary intervention; Q1: first quartile; Q3: last quartile.

symptom onset and history of cardiovascular disease. With the EMS-PCI route taken as the reference route, the adjusted HR for the ED-PCI route was 0.77 and for the ED-transfer-PCI route was 0.67 (Table 4). Patients turning up at the ED (with or without transfer) accessed PCI later than those transported by EMS. The PCI referral route remained an independent predictor of symptom-onset-to-needle time even after adjustment for symptom-onset-to-contact time (adjusted HR for ED compared with EMS, 0.71) (Table 4).

Hospital status and activity levels were not associated with differences in symptom-onset-to-needle and symptom-to-contact time (Table 3).

Discussion

We report the analysis of symptom-onset-to-needle times in STEMI for different referral routes to a primary coronary intervention facility in the French context. In our data set

of 1217 patients admitted to hospital with STEMI symptoms, symptom-onset-to-needle time was strongly associated with referral routes of access to a PCI facility. STEMI patients who were transported by EMS to a PCI facility had a median symptom-onset-to-needle time of 186 (133–292) minutes, whereas those who made their own way to hospital experienced delays of 51–119 minutes (they accounted for approximately one-third of patients undergoing primary PCI).

The use of data collected for quality assessment of care provided several advantages compared with an ad hoc data collection process (i.e. setting up a dedicated study). Firstly, although the information needed to estimate referral route, symptom onset time or needle time is not routinely available in France, it was available in the quality data set. Secondly, it enabled us to constitute a large sample at no additional cost/time as the hospitals had already collected the data for their quality improvement process. Finally, in each hospital, the data were extracted from patient files

Table 4 Cox proportional hazard model for symptom-onset-to-needle time.

	Hazard ratio [95% CI]	
	Non-adjusted	Adjusted for symptom-onset-to-contact time
EMS-PCI route	Reference	
ED-PCI route	0.77 [0.64–0.92]	0.71 [0.59–0.86]
ED-transfer-PCI route	0.67 [0.52–0.86]	— ^a
Age	0.99 [0.99–1.00]	0.99 [0.99–0.99]
Onset during weekend	1.05 [0.92–1.19]	1.03 [0.88–1.19]
Onset at night	0.75 [0.66–0.85]	0.72 [0.63–0.83]
History of cardiovascular disease	1.08 [0.91–1.27]	1.02 [0.85–1.23]
Symptom-onset-to-contact time	—	0.99 [0.99–1.00]

CI: confidence interval; ED: emergency department; EMS: emergency medical services; PCI: percutaneous coronary intervention.

^a Transfer route excluded from analysis.

by trained professionals who were familiar with the process and who were assisted by cardiologists, according to precise instructions developed to ensure the reliability of quality of care assessments. Thus, it was guaranteed that the provided observational data was of good quality.

Our results thus confirm in the French context the shorter delays to PCI access with prehospital STEMI diagnosis already recorded in Italy (> 45-minute reduction) and in Denmark for access to balloon inflation (91-minute reduction) [10,11]. As reported and as could be expected, delays were longest for transfers [12–15]. Despite this result, we observed that the EMS-PCI route had a lower percentage of patients with a contact-to-needle time > 90 minutes, as per current guidelines, compared with patients making their way to the ED and referred to an on-site PCI facility. The difference between the results in terms of the EMS-PCI route being better for onset-to-needle time and the ED-PCI route being better for contact-to-needle time is explained by a larger percentage of patients in the EMS-PCI route group receiving PCI within 90–120 minutes of first medical contact. Although this is not in line with the current recommendations, which require patients to undergo thrombolysis if estimated contact-to-needle time is > 90 minutes, it is possible that EMS physicians prefer taking the risk of going slightly over the 90-minute threshold to bring their patient to the PCI facility instead of starting thrombolysis that would increase the EMS transportation time with risk of failure.

It is worthwhile to note that the observed times for patients transported by EMS in our study were lower than the average European time of 230 minutes reported in the Euro Heart Survey programme [14]. The French EMS-PCI referral route characteristics could explain these shorter delays. Indeed, the emergency physician who is sent by the EMS with the mobile intensive care unit makes prehospital diagnosis possible. In several programmes, regardless of whether prehospital diagnosis is made by an on-site qualified physician [5,6], an off-site physician receiving the electrocardiogram from the emergency technicians [4,16] or by trained emergency technicians [5,16,17], it has been associated with a reduction in reperfusion delay. The best strategy for prehospital diagnosis, however, remains open for debate; in particular, reperfusion times between on-site and off-site prehospital diagnosis based on electrocardiograms have never been compared. In France, physician-manned mobile units are sent for patients with a suspected STEMI as it is believed that quicker care can be delivered in case of complications, including cardiac arrest or cardiogenic shock. The French EMS-PCI referral route also enables the ED to be bypassed and advance warning of the imminent arrival of a patient to be given to the PCI facility by the EMS physician. Both of these characteristics reduced time to reperfusion in the North Carolina ED study [16], the Door-to-Balloon campaign [18] and the National Cardiovascular Data Registry-Acute Coronary Treatment and Intervention Outcome Network.

Study limitations

Our study has four potential limitations. Although the sample of participating hospitals included institutions of different size, status (public/private) and geographical location, the hospitals actively volunteered to participate in

the quality of care assessment. Thus the symptom-onset-to-needle delays may have been shorter in these voluntary hospitals than in others. This should not, however, have affected the observed differences in delay between referral routes.

One-third of eligible patients were excluded because of missing data. Excluded eligible patients differed significantly from included patients in several respects. We postulated that this might be due to differences in the quality of the patient medical records, as data were obtained by retrospective medical record extraction. Indeed, a greater proportion of patients with symptom onset at night were excluded, as recording of information in the medical record may be poorer at night. On the other hand, a smaller proportion of patients transported directly by EMS to a PCI facility were excluded, probably because of good direct communication between the EMS physician and the PCI staff and, consequently, better recording of information in the medical record. Overall, the effect of poor versus good hospital data availability on the symptom-onset-to-needle time is difficult to predict.

Few patient variables were available for introduction into our analysis because our data source included variables needed for quality of care assessment only. Use of random sampling and stratification in the regression analysis reduced the likelihood of large differences in patient characteristics. Indeed, there was no difference in the distribution of patient characteristics between referral routes.

We could not assess differences in mortality rates according to referral route because our quality assessment data included only process and not outcomes data. Our observed delay of 51–119 minutes was within the range of 61–120 minutes for which a mortality rate of 23.3% has been estimated [19]. Mortality could be much reduced if all patients with STEMI symptoms were managed by EMS.

Conclusion

Our analysis shows that quality of care assessment provides a good opportunity to assess symptom-to-needle times in STEMI in France and has confirmed that calling the EMS in order to be transported directly to a PCI facility is the quickest way to access primary PCI after onset of STEMI symptoms in the French context. This is in line with current recommendations. However, 30% of STEMI patients did not follow the recommended referral route and a substantial amount of patient transport by EMS had a contact-to-needle time greater than the recommended 90-minute threshold, suggesting that more effort should be put into enforcing the recommendation. The first result of the national STEMI indicator programme that will include every hospital in France will provide an opportunity to further examine this subject.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

- [1] Berger PB, Ellis SG, Holmes Jr DR, et al. Relationship between delay in performing direct coronary angioplasty and early clinical outcome in patients with acute myocardial infarction: results from the global use of strategies to open occluded arteries in Acute Coronary Syndromes (GUSTO-IIb) trial. *Circulation* 1999;100:14–20.
- [2] Cannon CP, Gibson CM, Lambrew CT, et al. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA* 2000;283:2941–7.
- [3] Terkelsen CJ, Sorensen JT, Nielsen TT, et al. Percutaneous coronary intervention related delay in ST-segment elevation myocardial infarction patients. *J Am Coll Cardiol* 2009;53:1244 [author reply 44–5].
- [4] Rao A, Kardouh Y, Darda S, et al. Impact of the prehospital ECG on door-to-balloon time in ST elevation myocardial infarction. *Catheter Cardiovasc Interv* 2010;75:174–8.
- [5] Steg PG, Cambou JP, Goldstein P, et al. Bypassing the emergency room reduces delays and mortality in ST elevation myocardial infarction: the USIC 2000 registry. *Heart* 2006;92:1378–83.
- [6] van de Loo A, Saurbier B, Kalbhenn J, et al. Primary percutaneous coronary intervention in acute myocardial infarction: direct transportation to catheterization laboratory by emergency teams reduces door-to-balloon time. *Clin Cardiol* 2006;29:112–6.
- [7] Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012;33:2569–619.
- [8] Corriol C, Grenier C, Coudert C, et al. The COMPAQH project: researches on quality indicators in hospitals. *Rev Epidemiol Sante Publique* 2008;56(Suppl. 3):S179–88.
- [9] Corriol C, Daucourt V, Grenier C, et al. How to limit the burden of data collection for Quality Indicators based on medical records? The COMPAQH experience. *BMC Health Serv Res* 2008;8:215.
- [10] Ortolani P, Marzocchi A, Marrozzini C, et al. Clinical impact of direct referral to primary percutaneous coronary intervention following pre-hospital diagnosis of ST-elevation myocardial infarction. *Eur Heart J* 2006;27:1550–7.
- [11] Sorensen JT, Terkelsen CJ, Norgaard BL, et al. Urban and rural implementation of pre-hospital diagnosis and direct referral for primary percutaneous coronary intervention in patients with acute ST-elevation myocardial infarction. *Eur Heart J* 2011;32:430–6.
- [12] Blankenship JC, Skelding KA, Scott TD, et al. Predictors of reperfusion delay in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention from the HORIZONS-AMI trial. *Am J Cardiol* 2010;106:1527–33.
- [13] Liebetrau C, Szardien S, Rixe J, et al. Direct admission versus transfer of AMI patients for primary PCI. *Clin Res Cardiol* 2011;100:217–25.
- [14] Nallamothu BK, Bates ER, Herrin J, et al. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRM)-3/4 analysis. *Circulation* 2005;111:761–7.
- [15] Wang TY, Nallamothu BK, Krumholz HM, et al. Association of door-in to door-out time with reperfusion delays and outcomes among patients transferred for primary percutaneous coronary intervention. *JAMA* 2011;305:2540–7.
- [16] Jollis JG, Roettig ML, Aluko AO, et al. Implementation of a statewide system for coronary reperfusion for ST-segment elevation myocardial infarction. *JAMA* 2007;298:2371–80.
- [17] Le May MR, Dionne R, Maloney J, et al. The role of paramedics in a primary PCI program for ST-elevation myocardial infarction. *Prog Cardiovasc Dis* 2010;53:183–7.
- [18] Krumholz HM, Bradley EH, Nallamothu BK, et al. A campaign to improve the timeliness of primary percutaneous coronary intervention: Door-to-Balloon: an alliance for quality. *JACC Cardiovasc Interv* 2008;1:97–104.
- [19] Terkelsen CJ, Sorensen JT, Maeng M, et al. System delay and mortality among patients with STEMI treated with primary percutaneous coronary intervention. *JAMA* 2010;304:763–71.